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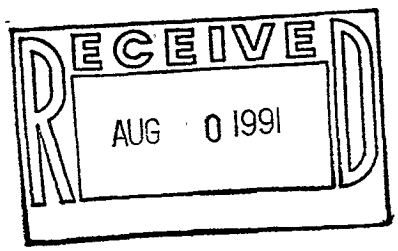

August 19, 1991

Council for Tobacco Research - USA, Inc.
900 Third Avenue
New York, NY 10022

Dear Sirs,

I am writing to inquire about a basic research grant in the areas of Cell Biology and Cancer-related Studies. My proposed project is, "Role of the IME2 Protein Kinase in Yeast Meiosis." An abstract follows.

Meiosis is the fundamental pathway of genetic transmission to progeny in all sexual eukaryotes. Our prior studies have established a hierarchy of meiotic regulatory genes in the budding yeast, *Saccharomyces cerevisiae*. The focus of this proposal is IME2, an activator of meiosis that stimulates entry both into S (DNA synthesis) phase and into M (Meiosis I) phase. The CDC28 product, a member of the ubiquitous p34-cdc2/MPF kinase family, is also required to enter M. The deduced IME2 product is a serine-threonine protein kinase with a 300 amino acid C-terminal domain of unknown function. Our studies of truncated IME2 products and of haploids forced into meiosis suggest that the C-terminal domain may regulate IME2 kinase activity in response to chromosome synapsis or recombination. We have recently found a rat gene (*mak*) through database searches that resembles *IME2* closely through the kinase domain. The *mak* transcript is expressed only in testes; thus *mak* and IME2 kinases may have conserved functions. Our plan is to identify substrates that are phosphorylated by IME2 through genetic and biochemical studies, to see whether IME2 phosphorylates CDC28 or vice-versa, to examine the role of synapsis and recombination in governing IME2 kinase activity, and to see whether the rat *mak* kinase can substitute for IME2 to activate S, MI, or both. Our goal is to elucidate meiotic regulatory signals and circuitry that may be widely conserved and of general importance in heredity and genetic diseases.

I hope that this project will be suitable for an application. I look forward to your response.

Sincerely,

Aaron Mitchell

Aaron P. Mitchell
Assistant Professor of Microbiology in
the Institute of Cancer Research

Source: https://www.industrydocuments.ucsf.edu/docs/ntmb0000